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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/068,160	02/06/2002	Dennis Klinman	4239-61997	9731

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KLARQUIST SPARKMAN, LLP
121 S.W. SALMON STREET, SUITE #1600
ONE WORLD TRADE CENTER
PORTLAND, OR 97204-2988

EXAMINER	
NGUYEN, DAVE TRONG	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/068,160	KLINMAN ET AL.	
	Examiner	Art Unit	
	Dave T Nguyen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-7,9,10 and 12-22* is/are rejected.

7)☐ Claim(s) *8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11/18/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claims 23-59 have been canceled by the amendment filed November 3, 2003. Applicant's election of the species SEQ ID NO: 1, and the species liposome in the response filed November 3, 2004 is acknowledged. Given that the prior art of record does not teach or suggest SEQ ID NO: 1, which exhibits a property of particularly stimulating production of more natural killer cells, monocytes, thereby leading to maturation of dendritic cells, relative to that of other CpG motifs known in the prior art such as those of K oligos, and of cytokines such as IP-10, IL-10, IFN-alpha, and IFN-gamma, a search of prior art was extended to SEQ ID NO: 35 as recited claim 12.

Claim 11 has been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species.

Claims 1-10, and 12-22 are pending for examination.

While the US patent documents and Foreign patent Documents have been considered, the references have not been initialed because the citations are not complete in the PTO-1449, *e.g.,* missing corresponding publication dates and author names.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 9, 12-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krieg (US Pat No. 6,207,646).

Krieg teaches a concept of utilizing an unmethylated CpG motif containing oligo having a modified phosphate backbone in order to stimulate an immune response for therapeutic applications of antigens and/or DNA *in vivo,* see column 11, last par. of column 12, for example. Krieg teaches on column 16, for example, that the unmethylated CpG mofif containing oligos if having palidrdomic flanking residues, are expected to be active in providing an immunostimulating effect. Krieg further teaches that (last par. of column 12) the preferred oligos should have the sequence TCAACGTT, which contains the self complementary "palindrome" AACGTT, as recited in applicant's claimed SEQ ID NO: 35. Krieg further teaches on column 12 that the oligos if containing poly-G at both ends, *e.g.,* GG at the 5' end and GGGG at the 3' end, the oligos would exhibit an additional immune-stimulating effect. By having a phosphorothioate modified poly G at the two ends, Krieg

teaches that the oligos are expected to cause an average 25.4 fold increase in mouse spleen cell proliferation compared to an average 3.2 fold increase in proliferation induced by ODNs not having the modified poly-G. Furthermore, Krieg teaches specifically that the preferred flanking residues are GpT and GpT, which are immediately positioned next to the CpG motif, such as SEQ ID NO: 31, which also folds within the generic formula set forth in claim 1, is one of the preferred CpG containing oligo motif. With respect to a stimulation of monocytes, natural killer cells, and dendritic cells, Krieg teaches on column 13 that an incorporation of a phosphate backbone modifications such as a phos-phorothioate or phosphodiester modification(s) would enhance productions of such cells. Delivery carriers including those of liposomes and/or targeting ligands, and pharmaceutically acceptable carriers are well-known in the prior art and taught throughout the Krieg reference, column 12.

As such, it would have been obvious for one of ordinary skill in the art to have further modified any taught CpG containing oligo in Krieg by incorporating a phosphorothioate modified poly-G at the ends of any of the taught oligos, such as palidromic sequences comprising any combination of palidromic residues flanking a CpG motif, and non-palidromic flanking residues containing CpG motif, such as the GTCGGT sequence, *e.g.,* SEQ ID NO: 31. One of ordinary skill in the art would have been motivated to do so because Krieg teaches the incorporation would cause multi-fold increase in mouse spleen cell proliferation, thereby leading to more production of desired production B cells.

It would also have been obvious for one of ordinary skill in the art to have further incorporated the sequence TCAACGTT, which contains the self complementary

"palindrome" AACGTT, in either the modified poly-G containing GTCGGT containing oligo sequence. One would have been motivated to do so because Krieg specifically teaches that by having the TCAACGTT motif in the oligos, which are taught to preferably have a length up to 100 nucleotide residues, the oligos are expected to have the most immunostimulatory effect, compared to those oligos that do not have the motif. Given the fact that Krieg teaches that as long as the immunostimulating CpG/poly G containing oligos are preserved within the context of the teachings of the immunostimulating motifs, any modifications of other nucleotide residues flanking the taught motifs are not expected to reduce the stimulation, and thus, are minor modifications and within the breadth of the claims, particularly since Krieg provides the general formula for the immunostimulating nucleic acids on column 11. Thus, it would be apparent to one of ordinary skill in the art that as long as a modified poly-G/CpG motif containing TCAACGTT sequence is preserved, any further incorporation of flanking residues such as those being recited in SEQ ID NO: 35 are expected to be a matter of obvious design choice, and thus, would have been obvious to one of ordinary skill in the art, particularly given the absence of an unexpected result with respect to those particular flanking residues.

Thus, the claimed invention as a whole was *prima facie* obvious.

Claim 8 is free of the prior art of record.

Claim 8 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **571-272-0731**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Amy Nelson*, may be reached at **571-272-0804**

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Trong Nguyen
Primary Examiner
Art Unit: 1632

DAVE T. NGUYEN
PRIMARY EXAMINER